

Supplementary Table I. Evolution of Therapy for Low Grade Glioma

Treatment Modality	Decade					Historic Treatment Modalities Used in Contemporary Therapy
	1960	1970	1980	1990	Post-2000	
Chemotherapy	▪ None			▪ Risk-Adapted (for symptomatic, progressive disease)		Risk-Adapted (symptomatic, progressive disease)
Agents				▪ Carboplatin ▪ Vincristine ▪ $\pm$ Temozolomide		Carboplatin Vincristine Temozolomide
Radiation	For localized and regional disease (20-40 Gy)			▪ Three-dimensional conformal radiation therapy		Three-dimensional conformal radiation therapy
Surgery	▪ Only for resectable cerebellar, cerebral hemisphere or thalamic tumors			▪ Only for resectable cerebellar, cerebral hemisphere or thalamic tumors and selected optic chiasm/hypothalamic or midbrain tumors		Only for resectable cerebellar, cerebral hemisphere or thalamic tumors and selected optic chiasm/hypothalamic or midbrain tumors

Supplementary Table II. Evolution of Therapy for Ependymoma

Treatment Modality	Decade					Historic Treatment Modalities Used in Contemporary Therapy
	1960	1970	1980	1990	Post-2000	
Chemotherapy	None				Incompletely resected disease – investigational only	Incompletely resected disease – investigational only
Agents		<ul style="list-style-type: none"> <li>▪ CCNU</li> <li>▪ Vincristine</li> </ul>				None
Radiation	Local or craniospinal Brain and spinal cord, if used (35-40 Gy) Primary tumor site (50-54 Gy)		Primary site (50-55 Gy)	Conformal, local primary site (50-55 Gy)	Conformal or IMRT – primary site (55-60 Gy)	Conformal– primary site (55 Gy)
Surgery	Total or subtotal resection					Total or subtotal resection

CCNU - 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea; IMRT – Intensity-modulated radiation therapy

Supplementary Table III. Evolution of Therapy for Retinoblastoma

Treatment Modality	Era		Historic Treatment Modalities Used in Contemporary Therapy
	Pre - 1990	Post - 1990	
Chemotherapy Agents	<ul style="list-style-type: none"> <li>For prevention of metastases in high risk patients: vincristine, cyclophosphamide, doxorubicin and other drugs used for embryonal tumors</li> <li>For metastatic and orbital disease in conjunction with radiotherapy</li> </ul>	<ul style="list-style-type: none"> <li>Carboplatin, etoposide, vincristine (CEV) with or without intrathecal methotrexate for prevention of metastases following enucleation in patients with massive choroidal and/or post-laminar involvement. CEV for chemo-reduction of large tumors prior to focal therapy.</li> <li>Two drugs (CV) for small intraretinal disease</li> <li>Topotecan/cyclophosphamide for resistant disease</li> <li>Intensive three-drug CEV with subconjunctival carboplatin for advanced disease to avoid enucleation and radiation.</li> <li>Autologous HCT following high dose chemotherapy for treatment of metastatic disease</li> </ul>	<ul style="list-style-type: none"> <li>Carboplatin</li> <li>Cyclophosphamide</li> <li>Etoposide</li> <li>Vincristine</li> </ul>
Radiation	<ul style="list-style-type: none"> <li>To preserve vision in bilateral advanced disease</li> <li>For bone metastases and orbital tumor</li> <li>To the CNS for tumor at the cut edge of the optic nerve following enucleation</li> </ul>	<ul style="list-style-type: none"> <li>As adjuvant following chemo-reduction and focal therapy to prevent recurrence or to treat recurrent active seeds</li> <li>Radioactive plaque for recurrent or resistant tumor</li> <li>Proton beam therapy under investigation</li> </ul>	<ul style="list-style-type: none"> <li>Following chemo-reduction and focal therapy to prevent recurrence</li> <li>To treat recurrent active seeds</li> <li>Radioactive plaque for recurrent or resistant tumor</li> </ul>
Dose	<ul style="list-style-type: none"> <li>40-44 Gy for primary intraretinal, orbital and metastases to bone.</li> </ul>	<ul style="list-style-type: none"> <li>25-35 Gy if used following chemo-reduction</li> </ul>	<ul style="list-style-type: none"> <li>25-35 Gy if used following chemo-reduction</li> </ul>
Focal therapy: Cryotherapy Thermotherapy	<ul style="list-style-type: none"> <li>For small tumors to avoid enucleation</li> </ul>	<ul style="list-style-type: none"> <li>Following chemo-reduction in advanced disease, to avoid enucleation and radiation</li> </ul>	<ul style="list-style-type: none"> <li>Following chemo-reduction in advanced disease, to avoid enucleation and radiation</li> </ul>
Surgery	<ul style="list-style-type: none"> <li>Enucleation the major treatment modality, especially for unilateral disease and for advanced bilateral disease not controlled by radiation</li> </ul>	<ul style="list-style-type: none"> <li>Enucleation for advanced unilateral disease remains the standard of care</li> <li>Enucleation for eyes with tumor unresponsive to chemo-reduction</li> <li>Biopsy and/or resection of orbital and metastatic disease</li> </ul>	<ul style="list-style-type: none"> <li>Enucleation for advanced unilateral disease remains the standard of care</li> <li>Enucleation for eyes with tumor unresponsive to chemo-reduction</li> <li>Biopsy and/or resection of orbital and metastatic disease</li> </ul>